

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
PARTICIPATION IN AUTOIMMUNE DISEASE
INVENTORS NAME: Henrik Ditzel et al.
SERIAL NO.: 09/828,708

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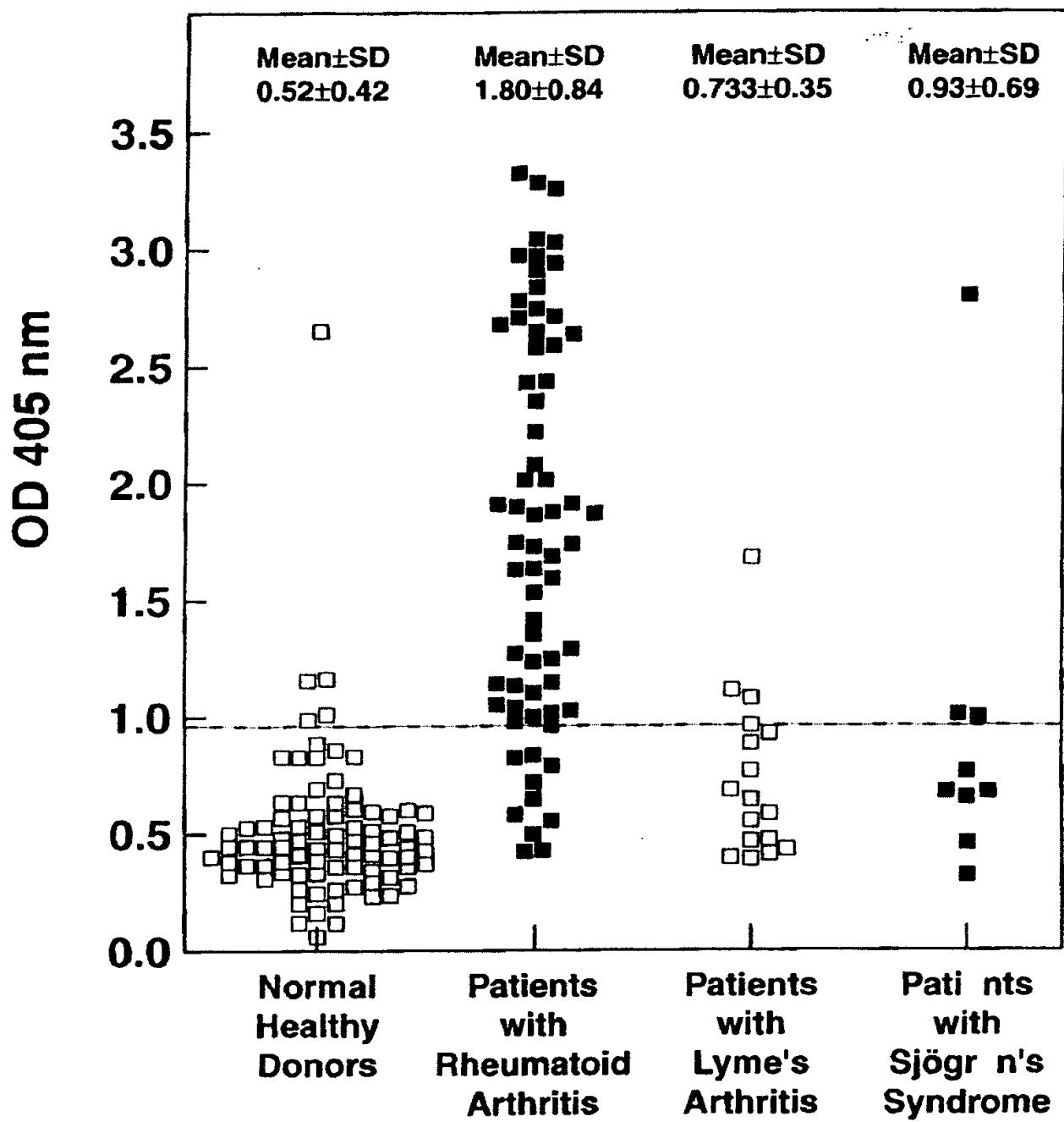


FIG. 1A

14.1.2007

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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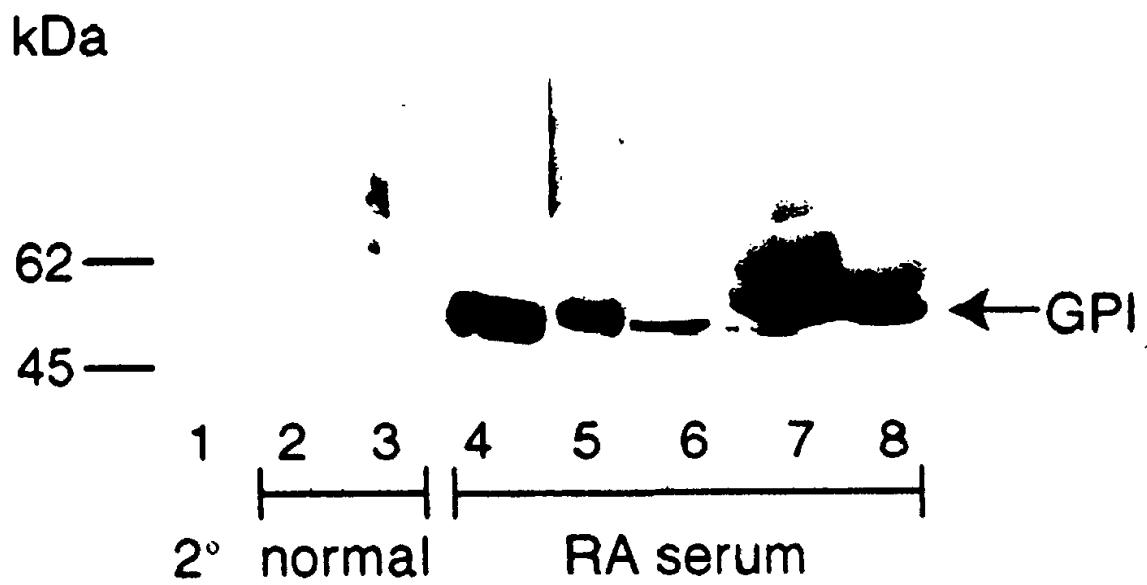


FIG. 1B

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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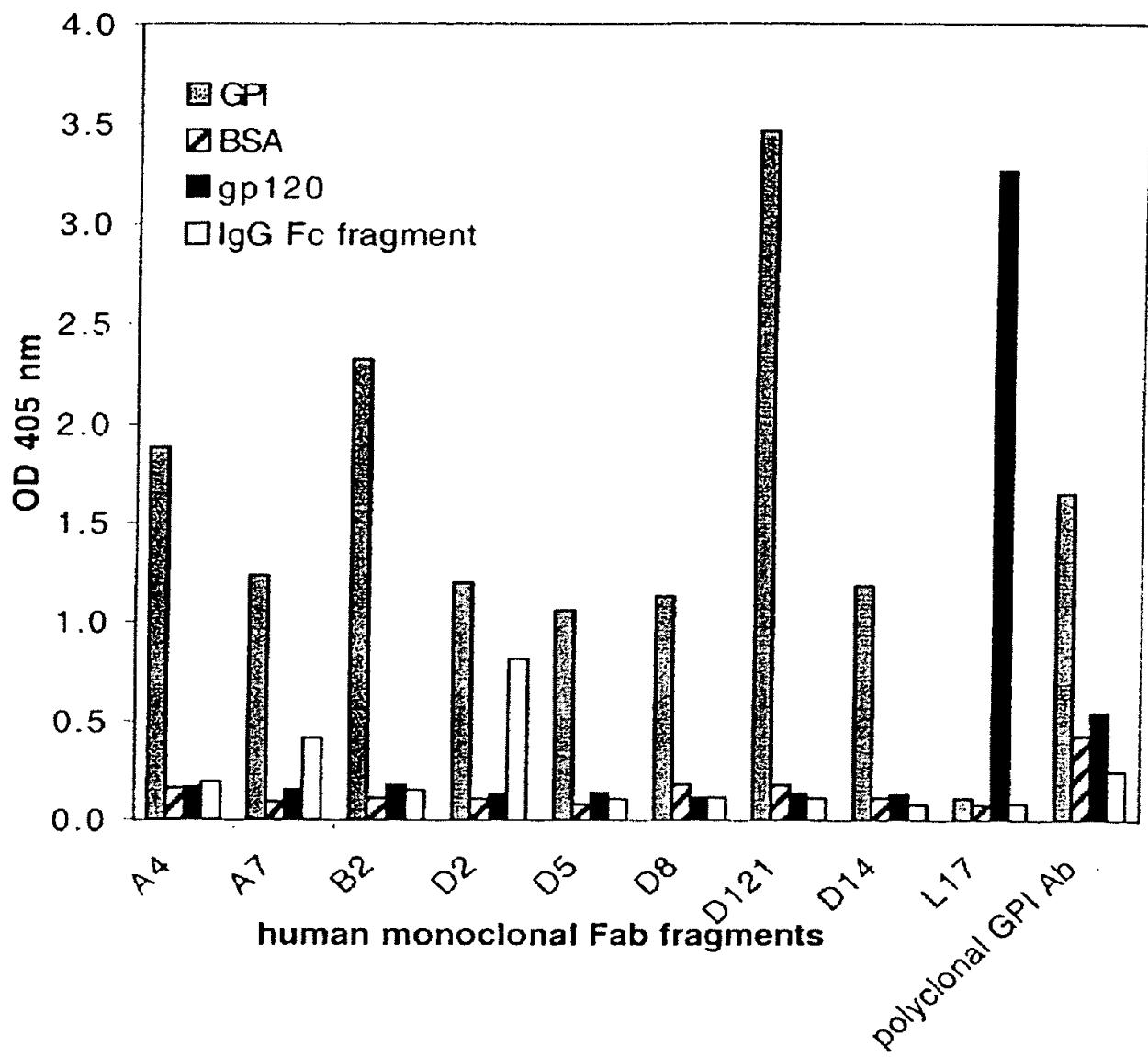


FIG. 2

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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Light Chain Variable AA Sequences

Name	SEQ ID NO:	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
A4	1	PDSLAVSLGERATINC	KSSQSVFYTSSNNKNYLA	WYQQKPGQQPKLLIY	WASTRES	GVPDRFSGSGSGTDFILTISLQAEDVAVYYC	QQYYDSYT	FGQGTKLEIKRTVA
	2	PSFLSASVGDRVTTTC	RASQGISSYLA	WYQLKPGKAPKLLIY				
	3	PGTLSSLSPGERATLSC	RASQSVSSSYLA	WYQQKPGQAPRLLIY				
B2	4	PDSLAVSLGERATINC	KSSQSVFYTSSNNKNYLA	WYQQKPGQQPKLLIY	WASTRES	GVPDRFSGSGSGTDFILTISLQAEDVAVYYC	QQYYDSYT	FGQGTKLEIKRTVA
	5	PGTLSLSPGEATLSC	RASQSVSSSYLA	WYQQRPGQAPRLLIY				
	6	PGTLSLSPGEATLSC	RASQSVSSSYLA	WYQQKPGQAPRLLIY				
D14	7	PGTLSLSPGERVTLSC	RASQSVSSSYLA	WYQQKPGQAPRLLIY	GASSRAT	GIPDRFSGSGSGTDFSTTISSLQPEDTGTYYC	QQYDNVPDT	FGQGTRLEIKRTVA
	8							
	9							
D2	10				GASSRAT	GIPDRFSGSGSGTDFITLTSRLEPEDFAVYYC	QQYGTSP	FGQGTRLEIKRTVA
	11							
	12							
D121	13				GASSRAT	GIPDRFSGSGSGTDFITLTSRLEPEDFAVYYC	QQYGSSPRT	FGQGTRLEIKRTVA
	14							
	15							
D5	16				GASSRAT	GIPDRFSGSGSGTDFITLTSRLEPEDFAVYYC	QQYGTSP	FGQGTRLEIKRTVA
	17							
	18							
A7	19				GASSRAT	GIPDRFSGSGSGTDFITLTSRLEPEDFAVYYC	QQYGSSPRT	FGQGTRLEIKRTVA
	20							
	21							

FIG. 3AL

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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Heavy Chain Variable AA Sequences

Name	SEQ ID NO.	FR1	CDR1	FR2	CDR2
A4	8	GGGVVQPGRLKLSCAAQSGFTFS	SHGSH	WVRQAPGKGLEWVA	LLSSDGSNKFYIESVKKG . TM.
D2	9AW..LR...V.....	..TM.TM.
D121	10R.....	YTF.	VI.Y..NK.Y.AD....
B2	11	GAEVRKPGBTSVRISCRASGNTFT	GHIIH	WVRQAPGQGLQWMG	RINPTGGVSLAQSFQD
D14	12	GGGLVQPGGSLRLSCATSGFIFN	SYAMN	WVRQAPGKGLEWVS	RISGNSGSTFYADSVKG
D5	13	GPGLVVRPSQTLTLCPVSPGSIK	GDYYFWS	WVRQPVGKGLEWIG	RIYGRGTTNYNRVFGS
A7	14	GAEVKKPQSSVVKVSCRASGGTFS	RYAIS	WVRQAPGQGLEWMG	GIIPPFGPVNIAQKFGQ
Name	cont'd	FR3	CDR3	FR4	VH gene
A4		RFTISKDN SKNTLILQMN SIRDDIAVYYCAI	SLVGTIAFNY	WGQGTIVTVSS	VH3
D2	R.....LS.....PE.....TN	E...A...D.	VH3
D121	VE.....	I.....	VH3
B2		RVSLTRDRSSNTVFILELSGLTEEDTALYFCAR	PRFNMI REPLDL	WGQGTIVTVSS	VH1
D14		RFTISR DN SKNTAFLRMNSQRAEDTA VYYCAK	DLSSGAYYYGMDV	WGQGTIVTVSS	VH3
D5		RVSM SVDMRSQFFLEL RDVT AADTA VYYCAR	DKGSEYSYFDP	WGQGIVVVNVFS	VH4
A7		RVTITADDSTNTAYMGLSSLRGDTA VYYCAR	VAYDGSGYYNNIPK1YYYSYMD	WGKGTTTVSS	VH1
			V		

FIG. 3AH

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Name	SEQ ID NO:	FR1	CDR1	FR2	CDR2
A4	8	GGGVQPGRSILKLSCAAASGFTFS	SHGSH	WVRQAPGKGLEWVA	LLSSDGSNKFYIESVKG
D2	9	...AW...LR...V.....	..TM.	..TM.	..TM.
D121	10R.....R.....	.YTF.	VI.Y..NK.Y.AD.	VI.Y.....AD.
DP-46	R.....R.....	.YAM.	VI.Y.....AD.	VI.Y.....AD.
B2	11	GAEVRKPGTSVRISCRASGNFT	GHHIH	WVRQAPGQGLQWMG	RINPTGGGVSLAQSFQD
DP-7		...K...A..KV.K..Y..	SYMMH	...E..	I...S..ST.Y..K..G
D14	12	GGGLVQPGSLLRSCATSGFIFN	SYAMN	WVRQAPGKGLEWVS	RISGNSGSTTFYADSVKG
VH26		...A...T.S	...S		A...SG...Y.....
D5	13	GPGLVVRPQRSTLTLCPVSPGSIK	GDSYFWI	WVRQPVGKGLEWIG	RIYGRGTTNNRNRFVGS
IGHCAK		...K.....T.G...S	SG..Y..	.I...A.....	...TS.S....PSLK.
A7	14	GAEVKKPQSSVKVSCRASGGTFS	RYAIS	WVRQAPGQGLEWMG	GIIPPFGPVNAYAQKFQG
VH1-69		...K.....	S...		...I..TA.....

FIG. 3B

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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Name cont'd	FR3	CDR3	FR4	VH Gene
A4	RFTISKDNSKNTLYLQMNSLRIDDTAVYYCAI	SLVGTAFNY	WGQGTLVTVSS	VH3
D2R.....LS...PE.....TN	.E..A...D.	VH3
D121VE.....	.I.....	VH3
DP-46R.....AE.....R	
B2	RVSLLTRDRSSNTVFILESGLTIEDDTALYFCAR	PRFNMIREPLDLI	WGQGTIVTVSS	VH1
DP-7	..TM...T.TS.YM...S.RS...V.Y...	DLSSGAYYYYGM	WGQGTTVTVSS	VH3
D14	RFTISRDNSKNTAFLRMNSQRaedDTAVYYCAK	DV	DV	
VH26LY.Q...L.....	
D5	RVSMSVDMSRSQFFLELIRDVIAADTAVYYCAR	DKGSEIYSYFDP	WGQGIIVNVFS	VH4
IGHCAK	..TI...T.KN..S.K.SS.....	
A7	RVTITADDSTNTTAYMGLSSLRSGDTAVYYCAR	VAYDGSGYNNI	WGKGTTIVTVSS	VH1
VH1-69K..S...E.....E.....	PKIYYYSYM DV	

FIG. 3B Cont'd

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Clone	Closest Germline	% amino acid homology	% nucleotide homology	R/S ratio FRs	R/S ratio CDRs
A4	DP-46	86	89	6/6:1.0	12/5:2.4
D2	DP-46	87	92	8/6:1.3	4/5:0.8
D121	DP-46	91	95	2/4:0.5	7/0:>7.0
B2	DP-7	67	79	20/17:1.2	<u>14/5:2.8</u>
D14	VH26	87	93	7/3:2.3	5/2:2.5
D5	IGHCAK	73	81	17/16:1.1	13/4:3.3
A7	VH1-69	90	94	7/2:3.5	5/0:>5.0

FIG. 3C

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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CDR's Heavy Chain

SEQ NO:	CDR1	SEQ ID NO:	CDR2	CDR3
15	SHGSH	22	LLSSDGSNKFYIYESVKG	2.9
16	.TM.	23	.IFY.....Y.AD....	3.0
17	.YTF.	24	VI.Y..NK.Y.AD....	3.1
18	GHHIH	25	RINPTGGGVSLAQSFQD	3.2
19	SYAMN	26	RISGNSGSTFYADSVKG	3.3
20	GDSYFWS	27	RIYGRGTTNNYNRVFGS	3.4
21	RYAIS	28	GIIPPFGPVNIAQKFAQG	3.5
SEQ ID NO:	CDR1	SEQ ID NO:	CDR2	CDR3
36	KSSQSVFYITSNNKNYLA	4.3	WASTRES	5.0
37	RASQGISSSYLA	4.4	AASTLQS	5.1
38	RASQSVSSSYLA	4.5	GASSRAT	5.2
39	KSSQSVFYITSNNKNYLA	4.6	WASTRES	5.3
40	RASQSVSSSYLA	4.7	GASSRAT	5.4
41	RASQSVSSSYLA	4.8	GASSRAT	5.5
42	RASQSVSSSYLA	4.9	GASSRAT	5.6

FIG. 4A

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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Framework Regions, Heavy Chain

SEQ ID	FR1	SEQ ID	FR2	SEQ ID	FR3	SEQ ID	FR4
NO:		NO:		NO:		NO:	
57	GGGVVQPGRSLLKSCAASGFTFS	64	WVRQAPGKGLEWVA	69	RFTISKDNSKNTLYLQMNSLRIDD TAVYYCAI	76	WGQGTIVTVSS
58AW..LR...V.....	64	70R.....LS...PE...TN	76
59R.....	64	71VE.....	76
60	GAEVRKPGTSVRISCRASGNFTF	65	WVRQAPGQGLQWMG	72	RVSLTRDRSSNTVFLFLE SGLTEEDTALYFCAR	77	WGQGTIVTVSS
61	GGGLVQPGGSLLRSCATSGFIFN	66	WVRQAPGKGLEWVS	73	RFTISRDNSKNTAFLRMNSQRAEDTAVYYCAK	78	WGQGTIVTVSS
62	GPGLVVRPSQTLSSLTCPVSPGSIK	67	WVRQPVVGKGLEWIG	74	RVSMSVDMRSQQFFELR DVTAA DTAVYYCAR	79	WGQGIVVVVVS
63	GAEVKPGSSVKVSCRASGGTFS	68	WVRQAPGQGLEWMG	75	RVTITADDSTNTAYMGLSSLRSGDTAVYYCAR	80	WGKGTTVTVSS

FIG. 4B

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATE ISOMERASE AND THEIR
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Framework Regions, Light Chain

SEQ ID NO:	FR1	SEQ ID NO:	FR2
81	PDSLAVSLGERATINC	88	WYQQKPGQPPKLLIY
82	PSFLSASVGDRTITC	89	WYQLKPGKAPKLLIY
83	PGTLSSLSPGERATLSC	90	WYQQKPGQAPRLLIY
84	PDSLAVSLGERATINC	91	WYQQKPGQPPKLLIY
85	PGTLSLSPGEGATLSC	92	WYQQRPGQAPRLLIY
86	PGTLSLSPGEGATLSC	93	WYQQKPGQAPRLLIY
87	PGTLSLSPGERVTLSC	94	WYQQKPGQAPRLLIY
SEQ ID NO:	FR3	SEQ ID NO:	FR4
95	GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC	102	FGQGTKLEIKRTVA
96	GVPDRFSGSGSGTTEFTLTSSLQPEDFAVYYC	103	FGGGAKVGIGRTVA
97	GIPDRFSGSGSGTDFLTISRLPEPDEFAVYYC	104	FGQGTKVEIKRTVA
98	GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC	105	FGQGTKLEIKRTVA
99	GIPDRFSGSGSGTDFSTISSLQPEDTGTYYC	106	FGQGTRLEIKRTVA
100	GIPDRFSGSGSGTDFTLTISRLEPDEFAVYYC	107	FGQGTRLEIKRTVA
101	GIPDRFSGSGSGTDFLTISRLPEPDEFAVYYC	108	FGQGTKVEIKRTVA

FIG. 4B Cont'd

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LIGHT CHAIN NUCLEOTIDE SEQUENCE OF ANTI-GPI ANTIBODIES

A4 - SEQ ID NO:112

CCAGACTCCCTGGCTCTGGGGAGAGGGCCACCATCAACTGCAAGTCCAGAGTGTCTTACACTTCCAAACAATAA
GAACATTAAGCTTGTTACCGAGCAGAAACCAGGCCAGCCTCCTAAAGTGTCTCATTACTGGGCATCCACCCGGGAATCCGGGGTCC
CTGACCGATTCAAGTGGCAGCGGGTCTGGGACAGATTCACTCTACCATCAGCAGCTGCAGGGCTGAAGATGGCAGTTATAC
TGTCAAGCAATATTATGATTCTGTACACTTTGGCCAGGGACCAAGCTGGAGATCAAAACGAACACTGTGGCT

D2 - SEQ ID NO:113

CCATCCTCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACCTGCCAGTCAGGCATTAGCAGTTAGCAGCTACTTCTAGGGTAT
CAGCTAAACCCGGAAAGCCCCCTAACGGCCTCAGCTGATCTATGCTGCATCTCCACTTGTCAAAGTGGGTCCATCAAGGTTCAAGGGCAG
TGGATCTGGGACAGAAATTCACTCTCACAAATAAGCAGCCTGCAGCCTGAAGATTTGCAACTTATTACTGTCAACAGCTAAATAGT
ACCCCTCACCTCGGGAGGGCCAAAGGTGGGATCAGACGAACACTGTGGCT

D121 - SEQ ID NO:114

CCAGGCACCCCTGTCTTGTCTCCAGGGGAAAGAGGCCACCCCTCTGCAGGGCCAGTCAGAGTGTCTAGGAGCTACTTCTAGGCTG
GTACCAAGCAGAAACCTGGCCAGGGCTCCAGGCTCCTCATCTATGGCATTCCAGCAGGGCAGCTGGCATCCCAGACAGGTTCAAGT
GCAGTGGGTCTGGGACAGACTTCACCTCACCATCACAGAGACTGGAGCCCTGAAGATTITGCAGTGTATTACTGTCAAGCTGGCT
AGCTCACCTCGGACGTTGGCCAAGGGACCAAGGTGGAAATCAAACGAACACTGTGGCT

B2 - SEQ ID NO:115

CCAGACTCCCTGGCTCTGGGGAGAGGGCCACCATCAACTGCAAGTCCAGAGTGTCTTACACTTCCAAACAATAA
GAACATTAAGCTTGTTACCGAGCAGAAACCAGGCCAGGCTCTAAAGTGTCTCATTACTGGGCATCCACCCGGGAATCCGGGGTCC
CTGACCGATTCAAGTGGCAGCGGGTCTGGGACAGATTCACTCACCATCAGCAGCTGCAGGCTGAAGATGTGGCAGTTATAC
TGTCAAGCAATATTATGATTCTGTACACTTTGGCCAGGGACCAAGCTGGAGATCAAAACGAACACTGTGGCT

FIG. 5A

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D14 - SEQ ID NO:116

CCAGGCACCCCTGTCTTCAGGGAAAGGCCACCCCTCTGCAGGGCCAGTCAGAGTGTAGCAGGCTACCTAGCCTG
GTATCAGCAGAACCTGGCCAGGCTCCAGGCTCATCTATGGTGCATCCAGCAGGGCACCCGCACTGGCATTCACTG
GAAGTGGATCTGGGACAGATTCAGTTCACTTCACCATCAGCAGTCAGGCTGAAGATACTGGGACATATTACTGTCAACAATATGAT
AATGTCCCTGACACTTGGCCAGGGGACCCAGGCTGGGAGATCAAACGAACACTGTGGCT

D5 - SEQ ID NO:117

CCAGGCACCCCTGTCTTCAGGGAAAGGCCACCCCTCTGCAGGGCCAGTCAGAGTGTAGCAGGCTACCTAGCCTG
GTACCAGCAGAACCTGGCCAGGCTCCAGGCTCCTCATCTATGGTGCATCCAGCAGGGCACTGGCATTCACTG
GCAGTGGGTCTGGGACAGACTTCACCTCACTTCACCATCAGCAGACTGGGACACTGGAGATTAACCGAACACTGTGGCT
ACCT CACCCCTCTGGCCAAGGGACACGACTGGAGATTAACCGAACACTGTGGCT

A7 - SEQ ID NO:118

CCAGGCACCCCTGTCTTCAGGGAAAGAGTCACCTCTGCAGGGCCAGTCAGAGTGTAGCAGGCTACCTAGCCTG
GTACCAGCAGAACCTGGCCAGGCTCCAGGCTCCTCATCTATGGTGCATCCAGCAGGGCACTGGCATTCACTG
GCAGTGGGTCTGGGACAGACTTCACCTCACTTCACCATCAGCAGACTGGGACACTGGAGATTAACCGAACACTGTGGCT
AGCTCACCTGGACCTGGGCCAAGGGACCAAGGTGGAAATCAAACGAACACTGTGGCT

FIG. 5A Cont'd

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HEAVY CHAIN NUCLEOTIDE SEQUENCE OF ANTI-GPI ANTIBODIES

A4-H - SEQ ID NO:116

D2-H - SEO ID NO:1117

GGGTGGTCCAAGGATGGAGGTCCCTAAGACTCTCCIGTGAGCTGTTGATTACCTTCAGTAGTCATACCATGCAACTGGGTCCG
CCAGGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCACTTATATTCTATGTAATAACTATGCGAAGTCCCGTGAAGGGC
CGATTCACCATCTCCAGAGACAATTCAAGAACACGCCTGCAATTGAGCAGGCTTAAGACCTGAGGACACGGCTGTCTTAA
TTGTACGAATTCGGAGTGGAGCTACCGCTTIGACTACTGGGGCAGGGAAACCCCTGGTCACCCGCTTCTCCAG

D1211-H-SEQ11 NO.118

GGGAGGGGTGGTCCAGCCTGGAGGTCCAGCCTGGATTCCACTTCACTTCACCTTGAGCTCTGG
GTCCGCCAGGCTCCAGGAAGGGCTGGAGTGGTGGCAGTTATCATATGATGGAAACAAGAAATACTACGAGACTCCGTGA
AGGGCCGATTCAACCATTCTCCAGAGACAATTCCAAGAACAATGAAACAGCCTGAGAGTGTAGGACACGGCTGT
TATTACTGTGCGATTCCATACTGGGAACACTACCGCTTAACTACCGCTTAACTACCGCTTACCGTCTCCCTC

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B2-H - SEQ ID NO:119

GGGGCTGAGGGTGAAGGAAGCCCCGACCTCCGTGAGGGATCCTTGCAACCTTCACTGCCACCATATTCACTG
GGTCGCCAGGGCCCTGGACAAGGGCCCTCAGTGGATGGGAAGAACATCAACCCGACTGGCGGGCTTAGTCTCGCACAGAGTTTC
CAGGACAGAGTCAGCCTGACCCAGGGACAGGTGTCAGTGGCTACGGGGCTAACAGTCTCAGTGGGAGACACGGCCT
TATATTCTGTGCAGGGCCCGATTAAACATGATCCGGAAACCTCTTGACCTCTGGGCCAGGGACAGTGGTCAACGTCTCCCTCA

D14-H - SEQ ID NO:120

GGGGGAGGCCCTGGTACAGCCTGGAGACTCTCCTGTGCAACCTCTGGATTCTGCATTAACAGCTATGCCATGAACCTG
GGTCGCCAGGGCTCCAGGGAAAGGGGCTTGAGTGGTCTCACGTATTAGTGGAAATAGTGGAAAGGCACATTCTACGCAGACTCCGTG
AAGGGCCGGTTCAACCATCTCCAGAGACAATTCCAAGAACAGGCCATTCTGGGAATGAACAGGCCAGAGGCCAACACGGCC
TTTATTACTGTGCAGAAAGATCTGTGAGTGGTGCATACTACTACGGGATGGACGTGGTCTGGGCCAAGGGACCACGGTCACCGTC
TCCTCA

D5-H - SEQ ID NO:121

GGCCCAGGGATTGGTGAAGGCCATCACAGACCCATCCCTCACCTGCACTGCTCCAGGGCTCCATTAAAGGTGATAGTTACTCTGG
AGCTGGGGTCCGTCAGCCGTAGGGAAAGGGACTGGAGTGGATAGGGCTATCTACGGCAGAGGGACTACCAATTACAACCGTGTGTT
TGGGAGTGTGAGTCAGTGTGACATGTGAGTCAGTGGTCAATTGAGAGATGTGACCTGAGTCAGTGGTCAATTGAGAGATGTGAGTCAGTGGTCAATTGAGAGATGTGGTCAACGGGTCCGAATACTCTACCTTGACCCCTGGGCCAGGGAAATAGTGGTCAACGTCTTCICA

FIG. 5B Cont'd

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A7-H - SEQ ID NO:122

GGGCTGAGGTGAAGAAGCCTGGGTCTCGGTGAAGGGTCTCCTGCAGGGCTTCAGCTGGCTTGACAAAGGCCCTGCGACAGGGCCATTACCGAGGTACGGATTCCACGGAAACACAGGCTACATGGGTCTGAGCAGCC
ACGCACAGAAGTTCCAGGGCAGAGTCCAGGCTGTTACTGGCGAGAGTGGCTATGATGGTAGTGGCTATTACAACAAATATCCCAA
TGAGATCTGGGACACAGGCCGTATTACTGGCTACATGGACGTCTGGCAAAAGGGACCAACGGTACCGTGTCCAGC
AGATCTACTACTACATGGACGTCTGGCAAAAGGGACCAACGGTACCGTGTCCAGC

FIG. 5B Cont'd

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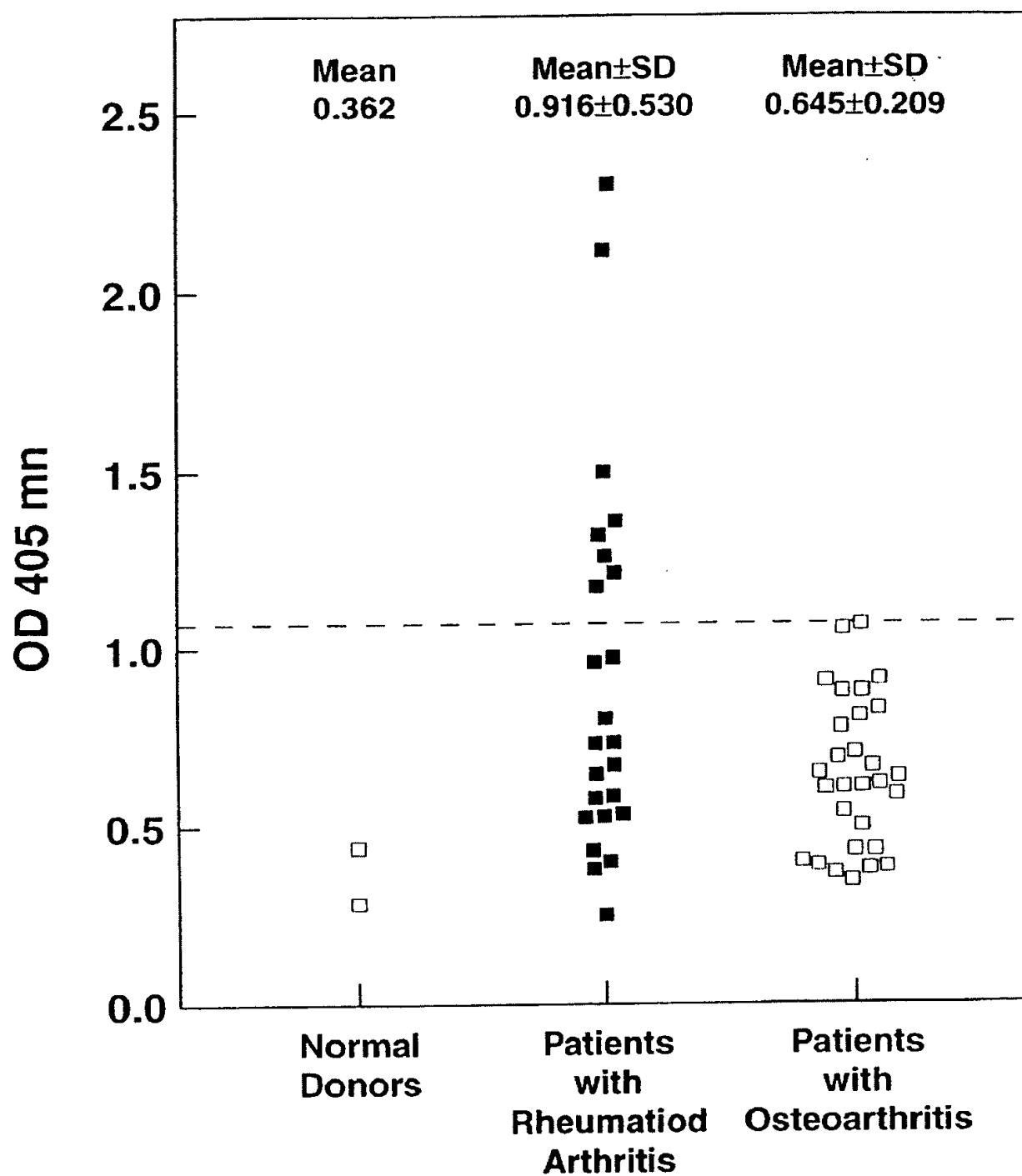


FIG. 6

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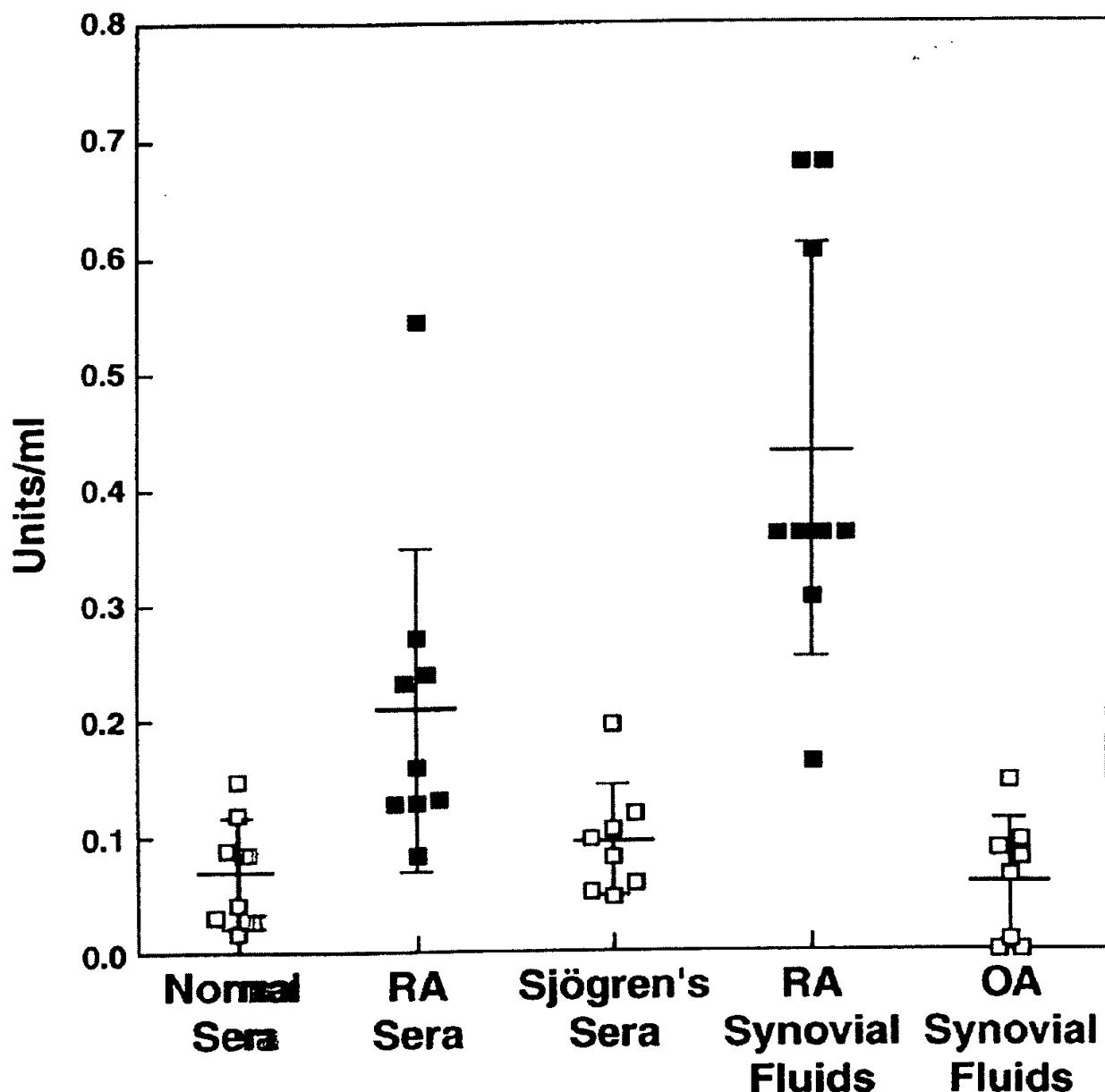


FIG. 7

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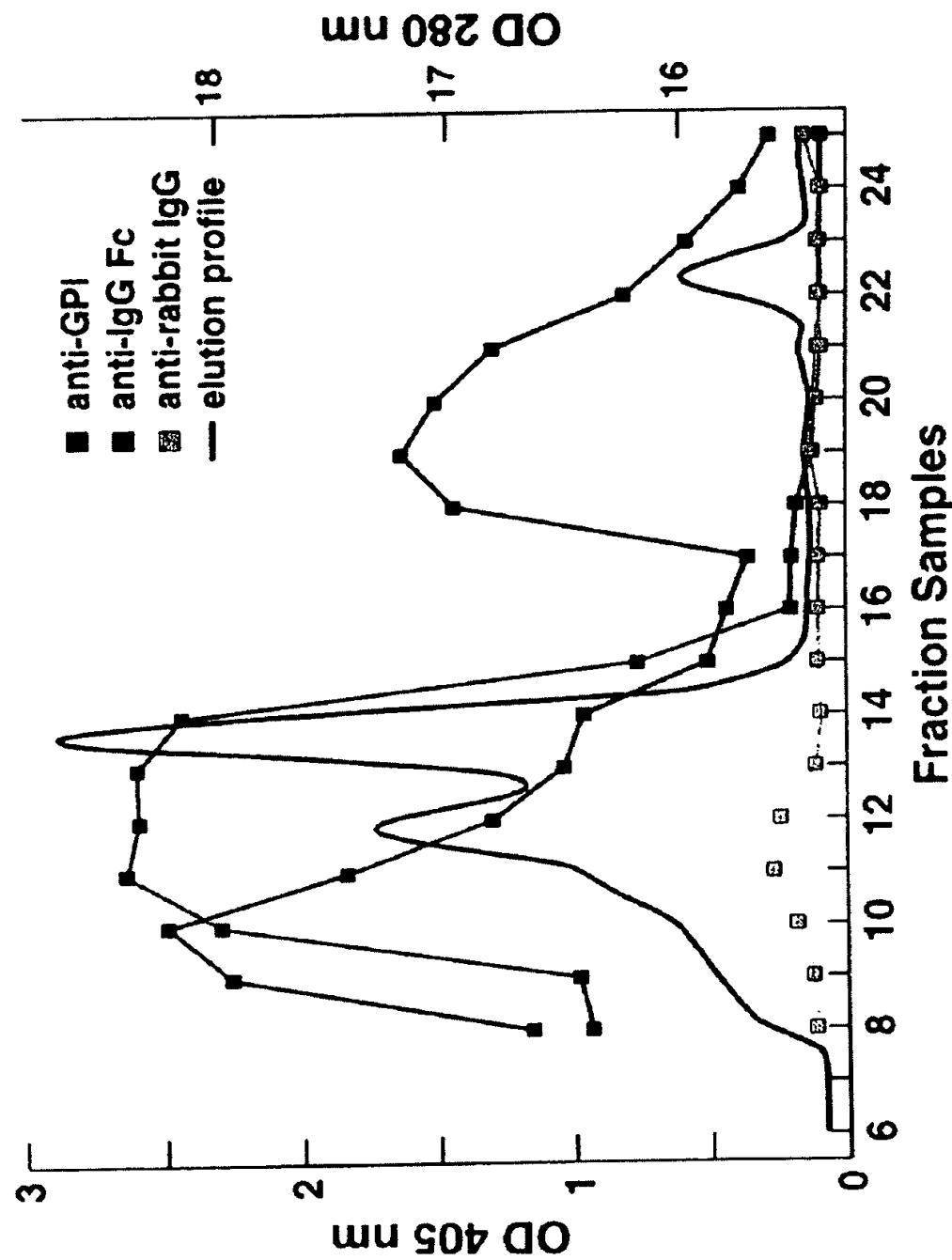


FIG. 8A

TITLE: AUTOANTIBODIES TO GLUCOSE-6-PHOSPHATOMERASE AND THEIR
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FIG. 8B



FIG. 8C

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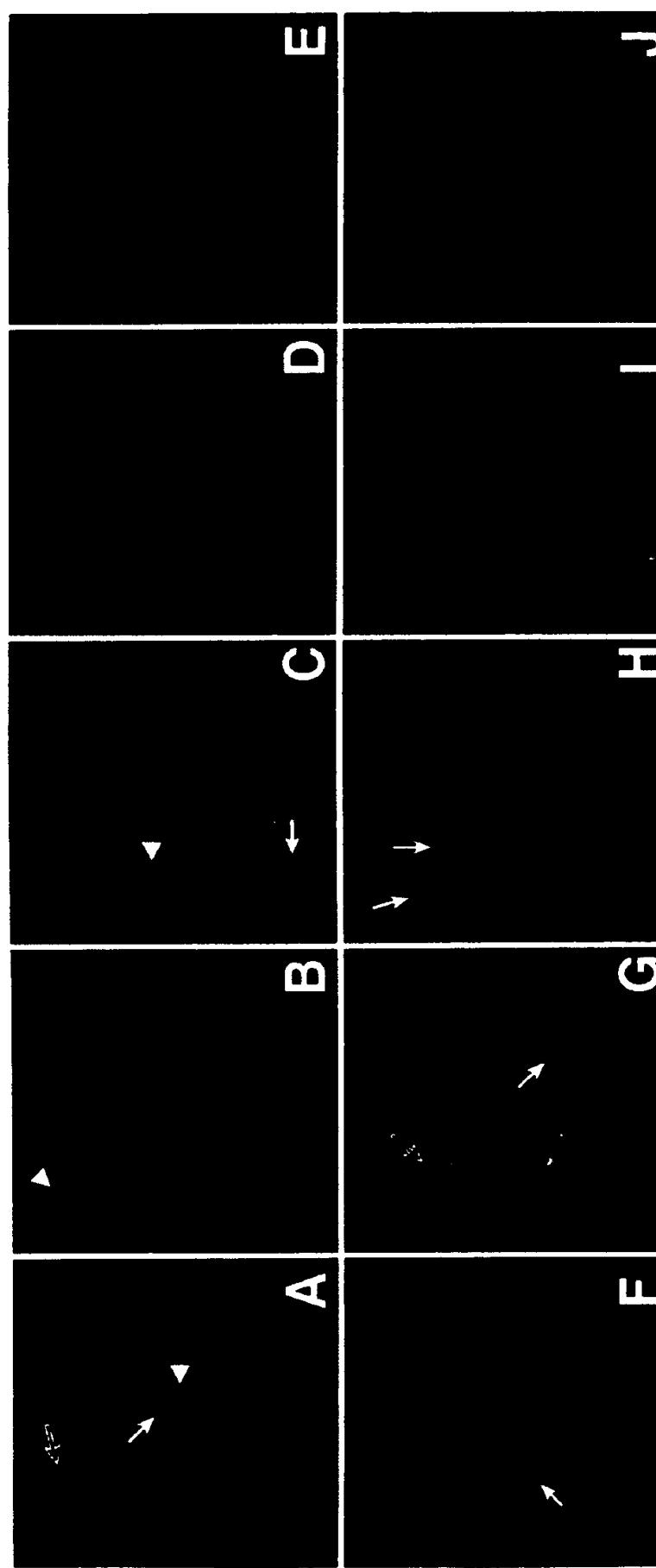


FIG. 9